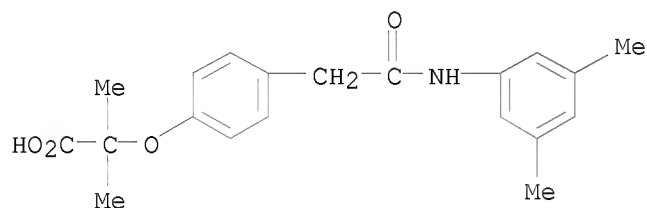


<http://www.cas.org/support/stngen/stndoc/properties.html>

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L1 1 EFAPROXIRAL/CN

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THE ESTIMATED COST FOR THIS REQUEST IS 2.10 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2010 ACS on STN
RN 131179-95-8 REGISTRY
ED Entered STN: 28 Dec 1990
CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl- (CA INDEX NAME)
OTHER NAMES:
CN 2-[4-[[[(3,5-Dimethylphenyl)amino]carbonyl]methyl]phenoxy]-2-methylpropionic acid
CN Efaproxiral
CN RSR 13
MF C20 H23 N O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

110 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
112 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
8.09	8.31

FILE 'CAPLUS' ENTERED AT 15:21:36 ON 19 MAY 2010
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 19 May 2010 VOL 152 ISS 21
 FILE LAST UPDATED: 18 May 2010 (20100518/ED)
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2010
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2010

CAPLUS now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2010.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s 12 and ( water or ethanol or acetone)
      3071740 WATER
      364953 ETHANOL
      208948 ACETONE
L4      7 L2 AND ( WATER OR ETHANOL OR ACETONE)

=> s 14 and py<2005
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L5      5 L4 AND PY<2005

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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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THE ESTIMATED COST FOR THIS REQUEST IS 29.05 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1995:758997 CAPLUS
DOCUMENT NUMBER: 124:55568
ORIGINAL REFERENCE NO.: 124:10501a,10504a
TITLE: Substituted 2-methyl-2-phenoxypropionic acid
derivatives as allosteric hemoglobin modifiers to
decrease oxygen affinity in blood
INVENTOR(S): Abraham, Donald J.; Mahran, Mona; Mehanna, Ahmed;
Randad, Ramnarayan; Joshi, Gajanan S.; Panikker,
Jayashree
PATENT ASSIGNEE(S): Center for Innovative Technology, USA
SOURCE: U.S., 24 pp. Cont.-in-part of U.S. 5,290,803.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5432191	A	19950711	US 1993-101501	19930730 <--
US 5049695	A	19910917	US 1990-478848	19900212 <--
US 5122539	A	19920616	US 1991-702947	19910520 <--
US 5382680	A	19950117	US 1991-722382	19910626 <--
US 5290803	A	19940301	US 1993-6246	19930119 <--
US 5731454	A	19980324	US 1995-374206	19950118 <--
US 5591892	A	19970107	US 1995-451658	19950530 <--
US 5648375	A	19970715	US 1995-478372	19950607 <--
US 5661182	A	19970826	US 1995-478108	19950607 <--
US 5677330	A	19971014	US 1995-478371	19950607 <--
US 5705521	A	19980106	US 1995-482808	19950607 <--
US 5927283	A	19990727	US 1997-848485	19970508 <--
US 5872282	A	19990216	US 1998-41595	19980313 <--
PRIORITY APPLN. INFO.:			US 1990-478848	A2 19900212
			US 1990-623346	B1 19901207
			US 1991-702947	A2 19910520
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			US 1993-6246	A2 19930119
			US 1992-885721	A1 19920518
			US 1993-101501	A2 19930730
			US 1993-127587	B1 19930928
			US 1995-374206	A3 19950118
			US 1995-478371	A3 19950607

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 124:55568

AB A family of compds. R2XYZC6H4R1 where R2 is a substituted or unsubstituted aromatic compound, or a substituted or unsubstituted alkyl ring compound, or a substituted or unsubstituted phthalimide compound that incorporates X and Y where X is a carbonyl, Y is a nitrogen and R2 completes the phthalimide compound by being bonded to both X and Y, and where X, Y, and Z are CH2, NH, S, SO2, CO, O or N with the caveat that the X, Y, and Z moieties are each different from one another, and where R1 has the formula: OCR3R4CO2R5 where R1 can be connected to any position on the Ph ring, and R3 and R4

are hydrogen, halogen, Me, Et, Pr, iso-Pr, neopentyl, Bu, or substituted or unsubstituted aryl groups and these moieties may be the same or different, or alkyl moieties as part of an aliphatic ring connecting R3 and R4, and R5 is a hydrogen, halogen, C1-3 loweralkyl, or a salt cation, has been found to be useful for right-shifting Hb towards a low oxygen affinity state. The compds. are capable of acting on Hb in whole blood. In addition, the compds. can maintain the oxygen affinity in blood during storage and can restore the oxygen affinity of outdated blood. Thus, e.g., treatment of 4-HOC6H4CH2CO2H with SOCl2 and 3,5-dichloroaniline afforded the intermediate 4-HOC6H4CH2CONHC6H3Cl2-3,5; O-alkylation of the latter with acetone/CHCl3 afforded 4-(HO2CCMe2O)C6H4CH2CONHC6H3Cl2-3,5 which exhibited a P50 (mm Hg) of 87 for oxygen dissociation of normal Hb in intact human red blood cells vs. 27 for the red blood cells alone (P50 = the pressure when the scanned Hb sample is 50% saturated with oxygen).

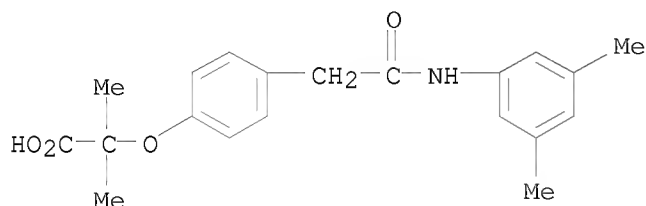
IT 131179-95-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(substituted 2-methyl-2-phenoxypropionic acid derivs. as allosteric Hb modifiers to decrease oxygen affinity in blood)

RN 131179-95-8 CAPLUS

CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1993:495107 CAPLUS

DOCUMENT NUMBER: 119:95107

ORIGINAL REFERENCE NO.: 119:17137a,17140a

TITLE: Preparation of phoxymethylpropionate derivatives as allosteric hemoglobin modifiers to decrease oxygen affinity in blood

INVENTOR(S): Abraham, Donald J.; Mahran, Mona; Mehanna, Ahmed; Randad, Ramnarayan

PATENT ASSIGNEE(S): Center for Innovative Technology, USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

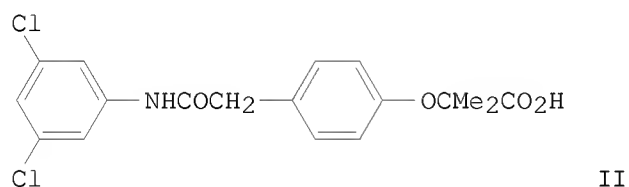
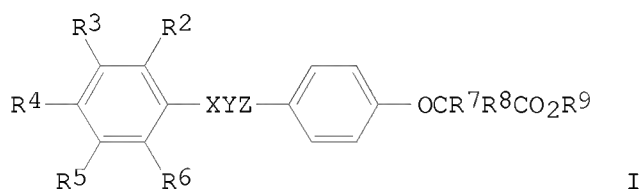
PATENT INFORMATION:

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WO 9220335	A1	19921126	WO 1992-US4229	19920519 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5122539	A	19920616	US 1991-702947	19910520 <--
US 5248785	A	19930928	US 1992-885721	19920518 <--
EP 585366	A1	19940309	EP 1992-912561	19920519 <--
EP 585366	B1	20040428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 07508973	T	19951005	JP 1993-500270	19920519 <--
JP 3023423	B2	20000321		
CA 2109575	C	20000201	CA 1992-2109575	19920519 <--
AT 265208	T	20040515	AT 1992-912561	19920519 <--
PRIORITY APPLN. INFO.:				
			US 1991-702947	A 19910520
			US 1992-885721	A 19920518
			US 1990-478848	A2 19900212
			WO 1992-US4229	W 19920519

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 119:95107

GI



AB Title compds. I (R2-R6 = H, halo, (substituted) C1-3 alkyl, C1-3 alkyl ether or ester, alkyl moieties of aromatic or aliphatic ring incorporating 2 of R2-R6 site; R7, R8 = H, Me, Et, etc.; R9 = H, halo, (substituted) C1-3 alkyl, cation salt; X, Y, Z = CH2, CO, NH, O) are prepared as allosteric Hb modifiers to decrease O affinity in blood. 4-HOC6H4CH2CO2H was refluxed with excess SOCl2, then reacted for 2 h with 3,5-Cl2C6H3NH2 to give after workup II, which showed a decrease in Hb-O affinity (i.e., increase in P50 value of 87 from control 19).

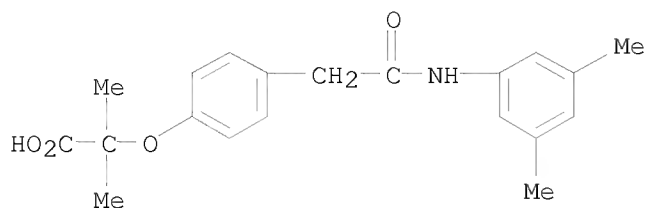
IT 131179-95-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for lowering oxygen affinity to Hb in blood)

RN 131179-95-8 CAPLUS

CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-

methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1993:45721 CAPLUS

DOCUMENT NUMBER: 118:45721

ORIGINAL REFERENCE NO.: 118:8119a,8122a

TITLE: Allosteric hemoglobin modifiers useful for decreasing oxygen affinity and preserving oxygen carrying capability of stored blood

INVENTOR(S): Abraham, Donald J.; Mahran, Mona; Mehanna, Ahmed; Randad, Ramnarayan

PATENT ASSIGNEE(S): Center for Innovative Technology, USA

SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 5,049,695.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5122539	A	19920616	US 1991-702947	19910520 <--
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CA 2051693	C	20050607		
US 5248785	A	19930928	US 1992-885721	19920518 <--
WO 9220335	A1	19921126	WO 1992-US4229	19920519 <--
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JP 3023423	B2	20000321		
CA 2109575	C	20000201	CA 1992-2109575	19920519 <--
EP 1236711	A2	20020904	EP 2002-12781	19920519 <--
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AT 265208	T	20040515	AT 1992-912561	19920519 <--

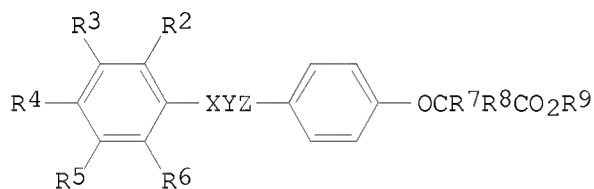
10/923,271

EP 1468680	A2	20041020	EP 2004-9908	19920519	<--
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US 5290803	A	19940301	US 1993-6246	19930119	<--
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US 5731454	A	19980324	US 1995-374206	19950118	<--
US 5591892	A	19970107	US 1995-451658	19950530	<--
US 5648375	A	19970715	US 1995-478372	19950607	<--
US 5661182	A	19970826	US 1995-478108	19950607	<--
US 5677330	A	19971014	US 1995-478371	19950607	<--
US 5705521	A	19980106	US 1995-482808	19950607	<--
US 5927283	A	19990727	US 1997-848485	19970508	<--
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			US 1992-885721	A	19920518
			EP 1992-912561	A3	19920519
			WO 1992-US4229	W	19920519
			US 1993-6246	A2	19930119
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			US 1995-374206	A3	19950118
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 118:45721

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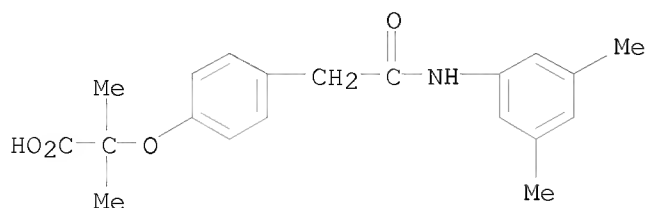
AB I (X,Y,Z = CH2, NH or O and R2-R6 = e.g., H, halo, substituted or unsubstituted C1-3 allyl, R7, R8 = H, Me or Et, R9 = H, alkyl, or metal salt) are prepared and have the ability to maintain oxygen affinity in blood during storage and can restore the O affinity of outdated blood. p-Acetaminophenol was treated with acetone and CHCl3 in NaOH solution and the acetaminophenoxymethylpropionic acid obtained after acidification was hydrolyzed and later acylated with an acid chloride such as phenylacetyl chloride. The compds. showed O carrying properties of stored blood.

IT 131179-95-8P
RL: PREP (Preparation)
(preparation of, as allosteric Hb modifier for decreasing oxygen affinity

and preserving oxygen carrying properties)

RN 131179-95-8 CAPLUS

CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1991:655817 CAPLUS

DOCUMENT NUMBER: 115:255817

ORIGINAL REFERENCE NO.: 115:43485a, 43488a

TITLE: Preparation of allosteric hemoglobin modifiers

INVENTOR(S): Abraham, Donald J.; Mehanna, Ahmed; Randad, Ramnarayan; Mahran, Mona

PATENT ASSIGNEE(S): Center for Innovative Technology, USA

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

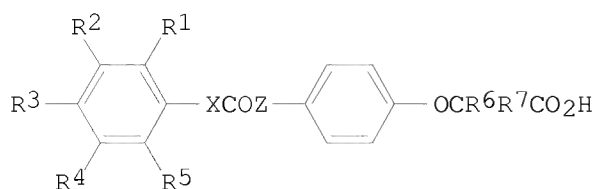
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CA 2051693	A1	19910813	CA 1991-2051693	19910206 <--
CA 2051693	C	20050607		
EP 471811	A1	19920226	EP 1991-904612	19910206 <--
EP 471811	B1	19951227		
R: DE, FR, GB, IT				
JP 04506812	T	19921126	JP 1991-504932	19910206 <--
JP 3023422	B2	20000321		

PRIORITY APPLN. INFO.: US 1990-478848 A 19900212
WO 1991-US833 W 19910206

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 115:255817; MARPAT 115:255817

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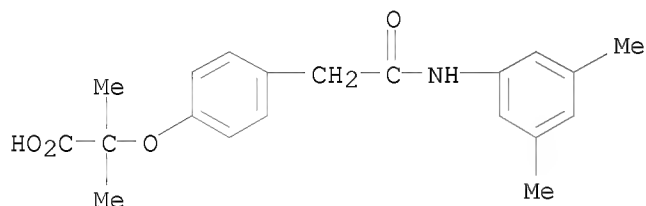


AB Title modifiers I [R1 - R5 = H, halo, (substituted) C1-3 alkyl; R6, R7 = H, Me; X, Z = CH2, NH, O, with the proviso that when X is CH2, Z is NH, when X is NH, Z is either CH2 or O, and when X is O, Z is NH] are prepared NaOH was added to p-(AcNH)C6H4OH in acetone, followed by addition of CHCl3, to give after acidification with HCl the appropriate (acetaminophenoxy)methylpropionic acid, which was treated with KOH to give 4-(H2N)C6H4OCMe2CO2H, which was dissolved with stirring in aqueous NaOH, and to this solution was added PhCH2COCl to give I (R1-R5 = H, R6 = R7 = Me, X = CH2, Z = NH) (II). The biol. activities of II and addnl. I are given.

IT 131179-95-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as allosteric Hb modifier)

RN 131179-95-8 CAPLUS

CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1991:81170 CAPLUS

DOCUMENT NUMBER: 114:81170

ORIGINAL REFERENCE NO.: 114:13837a,13840a

TITLE: Allosteric modifiers of hemoglobin. 1. Design, synthesis, testing, and structure-allosteric activity relationship of novel hemoglobin oxygen affinity decreasing agents

AUTHOR(S): Randad, Ramnarayan S.; Mahran, Mona A.; Mehanna, Ahmed S.; Abraham, Donald J.

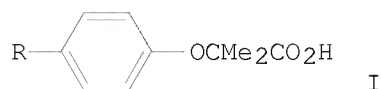
CORPORATE SOURCE: Dep. Med. Chem., Virginia Common. Univ., Richmond, VA, 23298-0581, USA

SOURCE: Journal of Medicinal Chemistry (1991), 34(2), 752-7

CODEN: JMCMAR; ISSN: 0022-2623

10/923,271

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:81170
GI



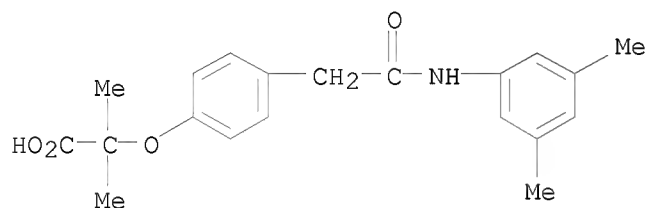
AB Three isomeric series of 2-aryloxy-2-methylpropionic acids I (R = R1CH2CONH, R1CONHCH2, R1NHCOCH2; R1 = Ph, substituted phenyl) were prepared and studied for their ability to decrease the oxygen affinity of human Hb A. Structure-activity relationships are presented. Several of the new compds. were strong allosteric effectors of Hb. The two most active compds. are I (R = 3,5-R22C6H3NHCOCH2; R2 = Cl, Me) (II). Compared to other known potent allosteric effectors, II show greater activity. II also exhibit a right shift in the oxygen equilibrium curve when incubated with whole blood.

IT 131179-95-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as allosteric effector of Hb)

RN 131179-95-8 CAPLUS

CN Propanoic acid, 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (45 CITINGS)

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